SPEAR PHARMACEUTICALS

To: Janet Woodcock, MD, Director FDA-CDER 12/29/99

Re: Guidance for Industry: Topical Dermatological Drug Product NDA's and ANDA's-In Vivo Bioavailability, Bioequivalence, in Vitro Release, and Associated Studies.

Dr. Woodcock:
I know that the above Draft guidance is on your desk for approval.
It must be a difficult decision for you and I am sure you are receiving different conflicting opinions on its merit.
I understand that a citizens petition has been filed against it and the Am. Acad. of Dermatology has sent a letter with reservations regarding its scientific merit.

On the pro side many members of the Generic Industry are lobbying for this saying it is the only way they can get approval of generic copies and that clinical studies are too difficult and costly to do.

As a Dermatologist and President of a Generic Research and Development company, I am uniquely qualified to enter my opinion.

High quality Generics can be developed under the current system and Bio-equivalence studies can be done to show equivalence. We have done this with our ANDA approvals for Retin-A Generics. We proved Bioequivalence by performing a 398 patient acne study on the highest strength(.1%) and a 412 patient acne study on the lowest strength(.025%). For waiver of the middle strength, we performed In vitro release of all 3 strengths Retin-A to our Generic Tretinoin. Our products are being sold as Geneva Tretinoin USP.
The secret to our success was to have a deformulation analysis so that we had all the inactive ingredients qualitatively identical and quantitatively as identical as we could. We also buy the identical active from BASF. We had it manufactured so that it was the same thickness (viscosity) to Retin-A.
Together, Geneva Pharmaceuticals and Spear Pharmaceuticals invested 1.2 million to receive approvals. These R and D costs are within reason for products of Retin-A's magnitude.

We have applications filed and expect approval soon on the .025% Tretinoin Gel.
It has been my experience that the office of Generic Drugs people have been very helpful and are interested in bringing high quality generics to the public.

In the Am. Acad of Derm position paper it quotes: " Dr. Franz compared 1% Hytone to generic 1% cortaid using the current FDA accepted vasoconstrictor assay as well as a cadaver skin assay. In both instances, Dr. Franz found the drugs to be different. However, when using tape stripping as the draft guidance requires and the first 2 strips are discarded and the next 10 strips are analyzed the drugs appeared to be the same." Not until strips 17 through 22 did they show differences.

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13100 PONDEROSA WAY ▪ FORT MYERS, FLORIDA 33907 ▪ 941-936-5098 ▪ FAX 941-936-5176

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The skin stripping technique is flawed, you might as well squeeze it out of the tube and measure the active ingredient, instead of putting it on the skin and peeling it off with tape and measuring it.

We have 3 other Generic drugs in the pipeline for clinical studies. We simply will repeat the clinical studies done by the Originator companies, obtained by FOI, to receive approval. If skin stripping is approved, we will not do clinical studies, we will do skin stripping. This would be an easier path for us, but not for the public a better path.

The point of my letter is to give you the perspective that Generic companies can do these human clinical studies, effectively and economically. That doing these will maintain and improve the quality of generics. I am seriously concerned that skin stripping will lower the quality of generics that the public is finally beginning to accept, expect and deserve.

Thank You,

Kim I. Spear M D Dermatologist
President Spear Pharmaceuticals

cc: Debbie Henderson Director Executive Operations to Dr. Woodcock
Above e-mail sent by Fax and mailed.

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